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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,154	12/26/2001	Toshiaki Tagawa	P21462	2932

7055 7590 04/24/2002

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RESTON, VA 20191

EXAMINER

COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 04/24/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/926,154

Applicant(s)

TAGAWA ET AL.

Examiner

Gary W. Counts

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 March 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                     | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                            | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>8-10</u> . | 6) <input type="checkbox"/> Other:  |

**DETAILED ACTION**

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 3 "sufficient" is vague. It is unclear what is to be considered sufficient. See deficiencies throughout the claims.

Claim 1, line 3 "substantially" is vague and indefinite. There is no definition of the term in the specification and it is unclear what is considered to be substantially. See deficiencies throughout the specification.

Claim 1, line 4 the recitation "even" is vague. The term is not a positive recitation, it is unclear if the ligand-bonded complex binds to a non-free target without the presence of a free target.

Claim 2, line 2 "of a same kind" is vague. It is unclear what applicant intends. Are the molecules of the same species? Do they have the same function or different functions?

Claim 11, line 2 the recitation "an active principle" is vague. It is unclear what applicant intends.

Art Unit: 1641

Claim 15 the recitation "wafer-soluble" is vague. It is unclear what applicant intends. Perhaps, Applicant intends water-soluble.

Claims 16 and 17 are vague and indefinite because of the use of acronyms: ie. E-7 M and E-8 M. Also these terms are not commonly used acronyms for dissociation constants. Also there is no definition for the terms in the specification. The terms should be defined in their first instance.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benz et al (US Patent 6,214,388) in view of Wands et al (US Patent 4,933,275).

Benz et al (US Patent 6,214,388) disclose liposomes (microparticles) which comprise a targeting moiety (ligand) which can be antibodies or antibody fragments (col 6, lines 39-51). Benz et al disclose that the targeting moiety specifically binds a characteristic marker of the target (col 6, lines 52-57). Benz et al disclose that these targeting moieties can be directly conjugated to the liposome (microparticle) (col 14, lines 31-33). Benz et al disclose that a water-soluble macromolecule, which can be polyethylene glycol is bonded to the liposome and that the targeting moiety (ligand) is attached to a part of the water-soluble macromolecule (col 3, line 46 – col 4, line 16) (see also col 8). Benz et al disclose that therapeutic agents can be stably entrapped in

Art Unit: 1641

liposomes at a suitable loading factor and administered at a therapeutically effective dose. Benz et al also disclose that these therapeutic agents may be anti-tumor agents (col 16, lines 64). Benz et al also disclose pharmaceutical compositions comprising the liposome-target moiety complex (ligand-bonded complex) (col 18, line 41 – col 19, line 50). Benz et al also disclose that about 50 to 100 of the ligand molecules per liposome are used (col 14, lines 29 and 30). Benz et al also disclose the use of anti-tumor antibodies.

Benz et al differ from the instant invention in failing to disclose the ligand of the ligand-bonded complex specifically binding to a non-free target even in the presence of a free target.

Wands et al (US Patent 4,933,275) disclose ligands (antibodies) which are specific for epitopes of a non-free target even in the presence of a free-target (col 4, lines 5-9, see also figure 1). The use of these ligands makes it possible to determine patient status with respect to certain neoplasms (col 2, lines 62-64). These ligands also provide the diagnostic capabilities to distinguish between hydatiform mole and choriocarcinoma development from normal pregnancy where increased production of free alpha or beta-hCG subunits have been reported (col 10, lines 28).

It would have been obvious to one of ordinary skill in the art to incorporate the use of specific ligands for specific epitopes as taught by Wands et al into the complex of Benz et al because Wands et al shows that the use of these ligands makes it possible to determine patient status with respect to certain neoplasms (col 2, lines 62-64). These ligands also provide the diagnostic capabilities to distinguish between hydatiform

Art Unit: 1641

mole and choriocarcinoma development from normal pregnancy where increased production of free alpha or beta-hCG subunits have been reported.

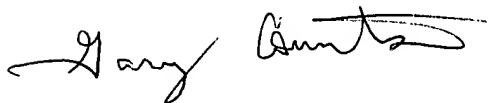
With respect to the dissociation constant between the target and one ligand as recited in the instant claims. Benz et al and Wands et al disclose the ligand-bonded complex as claimed and therefore, it would inherently comprise the dissociation constant between the target and one ligand as recited in the instant claims.

### ***Conclusion***

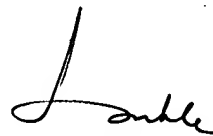
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Gary W. Counts  
Examiner  
Art Unit 1641  
April 10, 2002



LONG V. LE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

04/10/02